```
      12sep01 16:47:33 User217743 Session D535.1
        $0.00   0.207 DialUnits FileHomeBase
    $0.00  Estimated cost FileHomeBase
    $0.00  Estimated cost this search
    $0.00  Estimated total session cost   0.207 DialUnits
File 410:Chronolog(R)  1981-2001/Sep
     (c) 2001 The Dialog Corporation

    Set  Items  Description
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? set hi *;set hi *

HILIGHT set on as '*'*
*HILIGHT set on as '*'
? b 411

     12sep01 16:47:39 User217743 Session D535.2
        $0.00   0.066 DialUnits File410
    $0.00  Estimated cost File410
    $0.00  Estimated cost this search
    $0.00  Estimated total session cost   0.273 DialUnits File
411:DIALINDEX(R)

DIALINDEX(R)
  (c) 2001 The Dialog Corporation plc

*** DIALINDEX search results display in an abbreviated *** ***
format unless you enter the SET DETAIL ON command. *** ?
set files biochem

>>>       162 is unauthorized
>>>1 of the specified files is not available
  You have 25 files in your file list.
  (To see banners, use SHOW FILES command)
? s (connective()tissue()growth()factor or ctgf)


Your SELECT statement is:
  s (connective()tissue()growth()factor or ctgf)

       Items   File
       -----   ----
         294     5: Biosis Previews(R)_1969-2001/Sep W2
     2     6: NTIS_1964-2001/Sep W4
         273    34: SciSearch(R) Cited Ref Sci_1990-2001/Sep
W2             8    50: CAB Abstracts_1972-2001/Aug
          37    65: Inside Conferences_1993-2001/Sep W2
    135    71: ELSEVIER BIOBASE_1994-2001/Aug W1
         192    73: EMBASE_1974-2001/Sep W1
          45    76: Life Sciences Collection_1982-2001/Jul
    4    77: Conference Papers Index_1973-2001/Sep
28    94: JICST-EPlus_1985-2001/Aug W2
          10    98: General Sci Abs/Full-Text_1984-2001/Jul
     30   143: Biol. & Agric. Index_1983-2001/Jul            67
144: Pascal_1973-2001/Sep W2
         194   155: MEDLINE(R)_1966-2001/Oct W1
          14   156: Toxline(R)_1965-2000/Dec
          13   172: EMBASE Alert_2001/Sep W2
           1   305: Analytical Abstracts_1980-2001/Sep W2
     2   370: Science_1996-1999/Jul W3
         162   399: CA SEARCH(R)_1967-2001/UD=13511

  19 files have one or more items; file list includes 25 files.
?    rf

Your last SELECT statement was:
  S (CONNECTIVE()TISSUE()GROWTH()FACTOR OR
CTGF)

Ref       Items   File
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N1          294     5: Biosis Previews(R)_1969-2001/Sep W2 N2
        273    34: SciSearch(R) Cited Ref Sci_1990-2001/Sep
W2 N3          194   155: MEDLINE(R)_1966-2001/Oct W1
N4          192    73: EMBASE_1974-2001/Sep W1
N5          162   399: CA SEARCH(R)_1967-2001/UD=13511
N6          135    71: ELSEVIER BIOBASE_1994-2001/Aug
W1
N7           67   144: Pascal_1973-2001/Sep W2
N8           45    76: Life Sciences Collection_1982-2001/Jul N9
         37    65: Inside Conferences_1993-2001/Sep W2 N10
     30   143: Biol. & Agric. Index_1983-2001/Jul    19 files have
one or more items; file list includes 25 files.
      - Enter P or PAGE for more -
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Your last SELECT statement was:
  S (CONNECTIVE()TISSUE()GROWTH()FACTOR OR
CTGF)

Ref       Items   File
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N11         28    94: JICST-EPlus_1985-2001/Aug W2
N12         14   156: Toxline(R)_1965-2000/Dec
N13         13   172: EMBASE Alert_2001/Sep W2
N14         10    98: General Sci Abs/Full-Text_1984-2001/Jul
N15          8    50: CAB Abstracts_1972-2001/Aug
N16          4    77: Conference Papers Index_1973-2001/Sep
N17          2     6: NTIS_1964-2001/Sep W4
N18          2   370: Science_1996-1999/Jul W3
N19          1   305: Analytical Abstracts_1980-2001/Sep W2
N20          0    40: Enviroline(R)_1975-2001/Sep
  19 files have one or more items; file list includes 25 files.
      - Enter P or PAGE for more -
? b n3, n1

     12sep01 16:50:08 User217743 Session D535.3
        $2.03   1.627 DialUnits File411
    $2.03  Estimated cost File411
    $0.15  TYMNET
    $2.18  Estimated cost this search
    $2.18  Estimated total session cost   1.900 DialUnits
SYSTEM:OS  - DIALOG OneSearch
 File 155:MEDLINE(R)  1966-2001/Oct W1
 File   5:Biosis Previews(R)  1969-2001/Sep W2
      (c) 2001 BIOSIS

    Set  Items  Description
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? s (connective()tissue()growth()factor or ctgf)

       94157  CONNECTIVE
     1146693  TISSUE
     1363376  GROWTH
     1095654  FACTOR
         464
CONNECTIVE(W)TISSUE(W)GROWTH(W)FACTOR
         337  CTGF
    S1    488
(CONNECTIVE()TISSUE()GROWTH()FACTOR OR CTGF)
? s (connective()tissue()growth()factor or ctgf)/ti
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12646 CONNECTIVE/TI
228216 TISSUE/TI
437497 GROWTH/TI
338645 FACTOR/TI
297
CONNECTIVE/TI(W)TISSUE/TI(W)GROWTH/TI(W)FACTOR/TI
96 CTGF/TI
S2 340
(CONNECTIVE()TISSUE()GROWTH()FACTOR OR CTGF)/TI ? s s2 and (structure or fragment?)

340 S2
843308 STRUCTURE
398618 FRAGMENT?
S3 37 S2 AND (STRUCTURE OR FRAGMENT?)
? red

>>>Unrecognizable Command
? rd

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S4 25 RD (unique items)
? t s4/3,ab/all

4/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11520349 21379879 PMID: 11487529
Rho-dependent inhibition of the induction of *connective* *tissue* *growth* *factor* (*CTGF*) by HMG CoA reductase inhibitors (statins).
Eberlein M; Heusinger-Ribeiro J; Goppelt-Struebe M
Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestrasse 8, D-91054 Erlangen, Germany.
British journal of pharmacology (England) Aug 2001, 133 (7) p1172-80 , ISSN 0007-1188 Journal Code: B00
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
It was supposed that inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase (statins) might inhibit the expression of the fibrosis-related factor CTGF (connective tissue growth factor) by interfering with the isoprenylation of Rho proteins. The human renal fibroblast cell line TK173 was used as an in vitro model system to study the statin-mediated modulation of the *structure* of the actin cytoskeleton and of the expression of CTGF mRNA. Incubation of the cells with simvastatin or lovastatin time-dependently and reversibly changed cell morphology and the actin cytoskeleton with maximal effects observed after about 18 h. Within the same time period, statins reduced the basal expression of CTGF and interfered with CTGF induction by lysophosphatidic acid (LPA) or transforming growth factor beta. Simvastatin and lovastatin proved to be much more potent than pravastatin (IC(50) 1 - 3 &mgr;M compared to 500 &mgr;M). The inhibition of CTGF expression was prevented when the cells were incubated with mevalonate or geranylgeranylpyrophosphate (GGPP) but not by farnesylpyrophosphate (FPP). Specific inhibition of geranylgeranyltransferase-I by GTI-286 inhibited LPA-mediated CTGF expression whereas an inhibitor of farnesyltransferases FTI-276 was ineffective. Simvastatin reduced the binding of the small GTPase RhoA to cellular membranes. The effect was prevented by mevalonate and GGPP, but not FPP. These data are in agreement with the hypothesis that interference of statins with the expression of CTGF mRNA is primarily due to interference with the isoprenylation of RhoA, in line with previous studies, which have shown that RhoA is an essential mediator of CTGF induction. The direct interference of statins with the synthesis of CTGF, a protein functionally related to the development of fibrosis, may thus be a novel mechanism underlying the beneficial effects of statins observed in renal diseases.

4/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11490029 21303057 PMID: 11409888
Hydrogen peroxide is a novel inducer of *connective* *tissue* *growth* *factor*.
Park SK; Kim J; Seomun Y; Choi J; Kim DH; Han IO; Lee EH; Chung SK; Joo CK
Laboratory of Ophthalmology and Visual Science, The Catholic University of Korea, Seoul, Korea.
Biochemical and biophysical research communications (United States) Jun 22 2001, 284 (4) p966-71, ISSN 0006-291X Journal Code: 9Y8 Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Connective tissue growth factor (CTGF) has recently been described as a fibrogenic factor and is greatly induced by various extracellular stimuli, such as transforming growth factor-beta (TGF-beta), dexamethasone, and serotonin. CTGF induces collagen type I and fibronectin, and the deposition of such molecules leads to fibrotic disease in many tissues. Intracellular reactive oxygen species (ROS) are generated by extracellular stress conditions and are produced as by-products of cellular metabolism. Imbalanced cellular redox status is a potent pathogenic factor that leads to various degenerative diseases, including tissue fibrosis. Since CTGF is believed to play a crucial role in fibrotic disease formation in many tissues, we examined the role of ROS in CTGF gene expression in human lens epithelial cell line B3. The results showed that CTGF was induced by reactive oxygen species such as hydrogen peroxide and hydroxyl radicals. Next, we examined whether CTGF induction by ROS is via newly synthesized TGF-beta. The results showed that ROS directly induced CTGF mRNA not via the increased TGF-beta synthesis or activation. Next, we treated AG490, which is the well-known inhibitor of Janus kinase (JAK), with hydrogen peroxide. AG490 abrogated the CTGF induction by ROS in a dose-dependent manner. The results suggest that JAK-2/-3 seems to be involved in the enhanced CTGF mRNA expression by hydrogen peroxide. In this report, we present that hydrogen peroxide is a novel inducer of CTGF gene expression and that JAK-2/-3 activation seems to play a role in CTGF induction. Copyright 2001 Academic Press.

4/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11466228 21270368 PMID: 11376134
Identification of human ccn2 (*connective* *tissue* *growth* *factor*) promoter polymorphisms.
Blom IE; van Dijk AJ; de Weger RA; Tilanus MG; Goldschmeding R Department of Pathology, H04.312, University Medical Centre Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.

Molecular pathology (England) Jun 2001, 54 (3) p192-6, ISSN 1366-8714 Journal Code: CNW
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Connective tissue growth factor (CCN2; CTGF) is a newly identified growth factor, which is involved in the regulation of wound repair and fibrosis. Because there is variation among individuals with respect to tissue response to injury, genetic factors might be involved in the final outcome of tissue repair or scarring. For example, polymorphisms in the promoter region of genes, such as those encoding transforming growth factor beta1 (TGF-beta1), interleukin 10 (IL-10), and tumour necrosis factor alpha (TNF-alpha), influence transcriptional responses and are thought to contribute to the dysregulation of these genes in pathological conditions. AIM:To investigate whether the promoter region of the ccn2 (ctgf) gene contains polymorphic sequences that might account for differential expression. MATERIALS/METHODS: Seventy seven human DNA samples were sequenced-45 were from healthy controls and 32 were from patients with ischaemic heart disease (IHD)-using M13 tailed sequence specific ccn2 (ctgf) primers for amplification of a 600 bp *fragment* upstream of the transcription start site. Amplicons were bidirectionally sequenced with a dye primer M13 forward and reverse sequencing kit. RESULTS: A C to G substitution was identified at position -132 in one of the patients with IHD. Moreover, in five of the 32 patients with IHD and in six of the 45 healthy controls, a G to C polymorphism was found at position -447. These substitutions at -132 and -447 are thought to lie within predicted binding domains for the transcription factors Pbx-1 and MZF1, respectively. In addition, insertions at position -43 (G), -47 (C), -71 (G) and a C to T substitution at position -198 were found in all DNA samples compared with the published ccn2 (ctgf) promoter sequence. These corrections do not involve sequences predicted to function as transcription factor binding sites. CONCLUSION: Sequence analysis of the ccn2 (ctgf) promoter of 77 human DNA samples has revealed corrections and polymorphic sites. The latter lie within putative regulatory elements.

4/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11421666 21264424 PMID: 11278731
Static pressure regulates *connective* *tissue* *growth* *factor* expression in human mesangial cells.
Hishikawa K; Oemar BS; Nakaki T
Department of Pharmacology, Teikyo University School of Medicine, Tokyo 173-8605, Japan. hisikawa@med.teikyo-u.ac.jp
Journal of biological chemistry (United States) May 18 2001, 276 (20) p16797-803, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Connective tissue growth factor (CTGF) is overexpressed in a variety of fibrotic disorders such as renal fibrosis and atherosclerosis. Fibrosis is a common final pathway of renal diseases of diverse etiology, including inflammation, hemodynamics, and metabolic injury. Mechanical strains such as stretch, shear stress, and static pressure are possible regulatory elements in CTGF expression. In this study, we examined the ability of static pressure to modulate CTGF gene expression in cultured human mesangial cells. Low static pressure (40-80 mm Hg) stimulated cell proliferation via a protein kinase C-dependent pathway. In contrast, high static pressure (100-180 mm Hg) induced apoptosis in human mesangial cells. This effect was reversed by treatment with CTGF antisense oligonucleotide but not with transforming growth factor beta1-neutralizing antibody or protein kinase C inhibitor. High static pressure not only up-regulated the expression of CTGF, but also the expression of extracellular matrix proteins (collagen I and IV, laminin). This up-regulation of extracellular matrix proteins was also reversed by treatment with CTGF antisense oligonucleotide. As judged by mRNA expression of a total of 1100 genes, including apoptosis-associated genes using DNA microarray techniques, recombinant CTGF protein induced apoptosis by down-regulation of a number of anti-apoptotic genes. Overexpression of CTGF in mesangial cells by transient transfection had similar effects. Taken together, these results suggest that high blood pressure up-regulates CTGF expression in mesangial cells. High levels of CTGF in turn enhance extracellular matrix production and induce apoptosis in mesangial cells, and may contribute to remodeling of mesangium and ultimately glomerulosclerosis.

4/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11221714 21147977 PMID: 11250650
Expression and regulation of osteopontin and *connective* *tissue* *growth* *factor* transcripts in rat anterior pituitary.
Ehrchen J; Heuer H; Sigmund R; Schafer MK; Bauer K
Max-Planck-Institut fur Experimentelle Endokrinologie, PO Box 610309, D-30603 Hanover, Germany.
Journal of endocrinology (England) Apr 2001, 169 (1) p87-96, ISSN 0022-0795 Journal Code: I1J
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cell-cell interactions are important regulatory elements in anterior pituitary (AP) physiology. As model systems to study pituitary cell-cell interactions, AP cells kept either as monolayers or as organotypic reaggregate cultures were analyzed by differential display PCR. We identified six cDNA *fragments* (osteopontin (Opn), connective tissue growth factor (CTGF), alpha(v)-integrin, cathepsin H, lysozyme and O-acetyl GD(3) ganglioside synthase) that showed elevated expression in monolayers compared with reaggregate cultures and the AP. The adenohypophyseal mRNA expression of Opn and CTGF, two secreted signaling substances, was studied in more detail. In situ hybridization histochemistry revealed that Opn mRNA expression is restricted to a subpopulation of gonadotropes whereas CTGF hybridization signals could not be ascribed to any known cell type. Opn transcript levels were downregulated in the APs of lactating rats and decreased when rats received s.c. injections of 17beta-estradiol for 5 days. The mRNA expression was higher in male than in female rats and increased after gonadectomy. CTGF transcript levels were higher in male compared with female rats and were increased in pregnant rats and in rats treated for 5 days with triiodothyronine or dexamethasone. These results indicate that Opn and CTGF may be of physiological importance as local communication factors in the AP.

4/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10893346 20525415 PMID: 11071863
Characterization of a mouse *ctgf* 3'-UTR segment that mediates repressive regulation of gene expression.
Kondo S; Kubota S; Eguchi T; Hattori T; Nakanishi T; Sugahara T; Takigawa M
Department of Biochemistry and Molecular Dentistry, Okayama University Dental School, 2-5-1 Shikata-cho, Okayama 700-8525, Japan. Biochemical and biophysical research communications (UNITED STATES) Nov 11 2000, 278 (1) p119-24, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We isolated a small segment of the 3'-untranslated region (3'-UTR) in the mouse connective tissue growth factor (ctgf/fisp12) gene and evaluated its functionality. Comparison of the nucleotide sequences of human and mouse ctgf 3'-UTRs revealed a conserved small segment of 91 bases. The corresponding segments of the 3'-UTRs shared as much as 82.4% homology, whereas the overall homology between the 3'-UTRs was 71.8%. To study the functionality of the conserved segment, the corresponding region of mouse ctgf cDNA was amplified from NIH3T3 cells. When it was fused downstream of a marker gene, it showed remarkable repressive effects on gene expression. The repressive effect of the sense form was more prominent than that of the antisense form. Computer analyses of these sequence predicted stable secondary structures, suggesting that they act at the RNA level. The predicted structures of the sense and antisense forms appeared to be slightly different, which is consistent with the difference in repressive function. These findings defined the conserved small element in the mouse ctgf gene as a potent negative regulator of gene expression, which may act at a posttranscriptional level. Copyright 2000 Academic Press.

4/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10842450 20484756 PMID: 11032028
Identification of an RNA element that confers post-transcriptional repression of *connective* *tissue* *growth* *factor* /hypertrophic chondrocyte specific 24 (*ctgf*/hcs24) gene: similarities to retroviral RNA-protein interactions.
Kubota S; Kondo S; Eguchi T; Hattori T; Nakanishi T; Pomerantz RJ; Takigawa M
Department of Biochemistry and Molecular Dentistry, Okayama University Dental School, Japan.
Oncogene (ENGLAND) Sep 28 2000, 19 (41) p4773-86, ISSN 0950-9232 Journal Code: ONC
Contract/Grant No.: A143876, PHS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The repressive effect of the 3'-untranslated region (3'-UTR) in human connective tissue growth factor/ hypertrophic chondrocyte specific 24 (ctgf/hcs24) mRNA on gene expression had been demonstrated in our previous study. Here, we identified a minimal RNA element in the 3'-UTR, which acts as a cis-acting element of *structure*-anchored repression (CAESAR). Deletion analyses of the 3'-UTR led us to minimize the element of 84 bases at the junction of the coding region and the 3'-UTR. The minimized RNA segment is predicted, and actually capable of forming a stable secondary *structure* in vitro. Mutational analyses disclosed a significant relationship between the predicted *structure* and repressive effect. The utility of CAESAR as a post-transcriptional regulatory element was represented by the fact that steady-state mRNA levels were not affected by CAESAR linked in cis, while protein levels from such a chimeric gene were markedly reduced. Of note, the CAESAR sequence exerted no effect, when it was placed upstream of the promoter. Finally, RNA gel electromobility-shift analyses demonstrated a nuclear factor that interacts with the folded CAESAR. Taken together, it was uncovered that CAESAR of ctgf is a novel post-transcriptional structured RNA regulatory element, probably acting through direct interactions with a nuclear factor as observed in retroviral RNA elements with certain proteins.

4/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10573864 20213327 PMID: 10748267
Connective *tissue* *growth* *factor* induces apoptosis via caspase 3 in cultured human aortic smooth muscle cells.
Hishikawa K; Nakaki T; Fujii T
Department of Pharmacology, Teikyo University School of Medicine, Kaga 2-11-1, Itabashi-ku, Tokyo, Japan. hisikawa@med.teikyo-u.ac.jp European journal of pharmacology (NETHERLANDS) Mar 24 2000, 392 (1-2) p19-22, ISSN 0014-2999 Journal Code: EN6
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Connective tissue growth factor (CTGF) stimulates proliferation of fibroblasts and endothelial cells, but nothing is known about its role in smooth muscle cells. In this study, the effects of recombinant human CTGF (r-hCTGF, 0.5-10 microgram/ml) on cultured human aortic vascular smooth muscle cells were investigated. r-hCTGF significantly reduced cell viability, increased apoptosis, and augmented caspase 3 activity. Moreover, r-hCTGF-induced apoptosis was significantly inhibited by an antibody to CTGF and a caspase-3 inhibitor, Z-Asp(Ome)-Glu-(Ome)Val-Asp(Ome)-FMK. These results suggest that r-hCTGF activates caspase 3 and induces apoptosis.

4/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10475563 20076381 PMID: 10607888
Transforming growth factor-beta(1) induces apoptosis via *connective* *tissue* *growth* *factor* in human aortic smooth muscle cells.
Hishikawa K; Nakaki T; Fujii T
Department of Pharmacology, Teikyo University School of Medicine, Kaga 2-11-1, Itabashi-ku, Tokyo, Japan. hisikawa@med.teikyo-u.ac.jp European journal of pharmacology (NETHERLANDS) Dec 3 1999, 385 (2-3) p287-90, ISSN 0014-2999 Journal Code: EN6
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We examined the possible involvement of connective tissue

growth factor (CTGF) in the apoptosis induced by transforming growth factor-beta(1) (TGF-beta(1)) in human aortic vascular smooth muscle cells (HASC). In quiescent HASC, TGF-beta(1) induced the mRNA and protein of CTGF. A CTGF antisense oligonucleotide inhibited this induction. TGF-beta(1) significantly reduced cell viability and induced DNA *fragmentation*, and the CTGF antisense oligonucleotide reversed these effects. Moreover, TGF-beta(1) activated caspase 3 in HASC, and the CTGF antisense oligonucleotide reduced this activation. These findings show that CTGF plays a key role in the TGF-beta(1)-induced apoptosis in HASC.

4/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10434964 20069744 PMID: 10601320
Connective *tissue* *growth* *factor* induces apoptosis in human breast cancer cell line MCF-7.
Hishikawa K; Oemar BS; Tanner FC; Nakaki T; Luscher TF; Fujii T Department of Pharmacology, Teikyo University School of Medicine, Tokyo 173-8605, Japan. hisikawa@med.teikyo-u.ac.jp
Journal of biological chemistry (UNITED STATES) Dec 24 1999, 274 (52) p37461-6, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Connective tissue growth factor (CTGF) is a member of an emerging CCN gene family that is implicated in various diseases associated with fibro-proliferative disorder including scleroderma and atherosclerosis. The function of CTGF in human cancer is largely unknown. We now show that CTGF induces apoptosis in the human breast cancer cell line MCF-7. CTGF mRNA was completely absent in MCF-7 but strongly induced by treatment with transforming growth factor beta (TGF-beta). TGF-beta by itself induced apoptosis in MCF-7, and this effect was reversed by co-treatment with CTGF antisense oligonucleotide. Overexpression of CTGF gene in transiently transfected MCF-7 cells significantly augmented apoptosis. Moreover, recombinant CTGF protein significantly enhanced apoptosis in MCF-7 cells as evaluated by DNA *fragmentation*, Tdt-mediated dUTP biotin nick end-labeling staining, flow cytometry analysis, and nuclear staining using Hoechst 33258. Finally, recombinant CTGF showed no effect on Bax protein expression but significantly reduced Bcl2 protein expression. Taken together, these results suggest that CTGF is a major inducer of apoptosis in the human breast cancer cell line MCF-7 and that TGF-beta-induced apoptosis in MCF-7 cells is mediated, in part, by CTGF.

4/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10394967 20029685 PMID: 10562268
Overexpression of *connective* *tissue* *growth* *factor* gene induces apoptosis in human aortic smooth muscle cells.
Hishikawa K; Oemar BS; Tanner FC; Nakaki T; Fujii T; Luscher TF Cardiology, University Hospital Zurich, and Cardiovascular Research, Institute of Physiology, University Zurich, Switzerland, Department of Pharmacology, Teikyo University School of Medicine, Tokyo, Japan. Circulation (UNITED STATES) Nov 16 1999, 100 (20) p2108-12, ISSN 0009-7322 Journal Code: DAW
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Connective tissue growth factor (CTGF) is expressed at very high levels particularly in the shoulder of human atherosclerotic lesions but not in normal blood vessels. Thus, CTGF may be important in the regulation of vascular smooth muscle cell function in atherosclerosis, but its precise role remains elusive. METHODS AND RESULTS: Full-length CTGF cDNA driven by a cytomegalovirus promoter was transiently transfected into cultured human aortic smooth muscle cells (HASCs). Northern and Western analysis demonstrated that CTGF was overexpressed in these cells 48 hours after transfection. The effects of CTGF overexpression on cell proliferation were evaluated by [(3)H]thymidine uptake and cell count in quiescent HASCs or those stimulated with platelet-derived growth factor (PDGF). Although mock transfection showed no effect, CTGF overexpression significantly inhibited cell proliferation in cells stimulated by PDGF. Moreover, CTGF overexpression, but not mock transfection, significantly increased apoptosis as assessed by DNA *fragmentation* associated with histone, TdT-mediated dUTP biotin nick end-labeling, and appearance of hypodiploid cells by flow cytometry. CONCLUSIONS: Our results for the first time demonstrate that CTGF can also act as a growth inhibitor in human aortic smooth muscle cells at least in part by inducing apoptosis. This may be important for the formation and composition of lesions and plaque stability in atherosclerosis.

4/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10076856 99196126 PMID: 10098490
Connective *tissue* *growth* *factor* (IGFBP-rP2) expression and regulation in cultured bovine endothelial cells.
Boes M; Dake BL; Booth BA; Erondu NE; Oh Y; Hwa V; Rosenfeld R; Bar RS Department of Internal Medicine, Diabetes and Endocrinology Research Center, Veterans Administration Medical Center, The University of Iowa, Iowa City 52246, USA.
Endocrinology (UNITED STATES) Apr 1999, 140 (4) p1575-80, ISSN 0013-7227 Journal Code: EGZ
Contract/Grant No.: DK-25295, DK, NIDDK; DK-25421, DK, NIDDK; DK-51513, DK, NIDDK; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Media from large vessel endothelial cells (pulmonary artery, aorta) contained intact connective tissue growth factor (CTGF) and a dominant 19-kDa band. N-terminal analysis of the 19-kDa band showed sequence corresponding to CTGF amino acid 181-190, suggesting that the 19-kDa band represented a proteolytic *fragment* of CTGF. Intact CTGF was increased by cAMP but not by transforming growth factor-beta (TGFbeta). CTGF messenger RNA (mRNA) was not changed by cAMP nor TGFbeta. In two microvessel endothelial cells, mRNA was found at low levels by PCR and Northern analysis, but no CTGF protein was seen on Western analysis. In the microvessel cells, TGFbeta increased and cAMP did not change CTGF mRNA levels, with neither TGFbeta nor cAMP increasing CTGF protein. The discordance between protein and mRNA levels in large vessel and microvessel

endothelial cells was mostly explained by the effects of cAMP and TGFbeta on media proteolytic activity; in large vessel cells, cAMP inhibited degradation of CTGF, whereas in microvessel cells, TGFbeta and cAMP stimulated proteolytic activity against CTGF. We conclude that in large vessel endothelial cells, cAMP increased intact CTGF protein by inhibiting degradation of CTGF, whereas TGFbeta stimulated neither CTGF mRNA nor protein; in microvessel cells, TGFbeta increased CTGF mRNA, while both TGFbeta and cAMP stimulated CTGF degradation.

4/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09802884 98326297 PMID: 9661651
Identification of glycosylated 38-kDa *connective* *tissue* *growth* *factor* (IGFBP-related protein 2) and proteolytic *fragments* in human biological fluids, and up-regulation of IGFBP-rP2 expression by TGF-beta in Hs578T human breast cancer cells. Yang DH; Kim HS; Wilson EM; Rosenfeld RG; Oh Y
Dept. of Pediatrics NRC5, Oregon Health Sciences University, Portland 97201, USA.
Journal of clinical endocrinology and metabolism (UNITED STATES) Jul 1998, 83 (7) p2593-6, ISSN 0021-972X Journal Code: HRB Contract/Grant No.: CA 58110, CA, NCI; DK51513, DK, NIDDK Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Connective Tissue Growth Factor (CTGF) is a cysteine-rich peptide involved in human atherosclerosis and fibrotic disorders such as scleroderma. CTGF has considerable N-terminal sequence similarity with the insulin-like growth factor binding proteins (IGFBPs), including preservation of cysteines, and has been postulated to be a member of the IGFBP superfamily. Indeed, recent studies have shown that baculovirus generated CTGF, a secreted 38-kDa protein, binds IGFs in a specific manner, leading to the provisional renaming of CTGF as IGFBP-8 (or IGFBP-rP2). With immunoprecipitation and immunoblotting, using polyclonal anti-IGFBP-rP2 antibody generated against recombinant human IGFBP-rP2bac, IGFBP-rP2 can be identified in the serum-free conditioned media of Hs578T human breast cancer cells, as well as in various human biological fluids, such as normal sera, pregnancy sera, and cerebrospinal, amniotic, follicular and peritoneal fluids. Glycosylation studies with endoglycosidase F reveal that endogenous human IGFBP-rP2 is a secreted, glycosylated, approximately 32-38-kDa protein with 2-8-kDa of N-linked sugars and a 30-kDa core. There are 18- and 24-kDa proteins that appear to be IGFBP-rP2 degradation products. In Hs578T human breast cancer cells, transforming growth factor (TGF)-beta 2, a potent growth inhibitor for these cells, upregulates IGFBP-rP2 mRNA and protein levels. Expression of Hs578T IGFBP-rP2 is significantly increased by TGF-beta 2 treatment in a dose-dependent manner, with 2.5- and 6-fold increases in mRNA and protein levels, respectively, at a TGF-beta 2 concentration of 10 ng/ml. Our studies indicate that IGFBP-rP2 appears to be an important endocrine factor, and one of the critical downstream effectors of the critical downstream effectors of TGF-beta, similar to the role of IGFBP-3 in TGF-beta-induced growth inhibition in human breast cancer cells.

4/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09673289 98119879 PMID: 9449709
Expression of the Elm1 gene, a novel gene of the CCN (*connective* *tissue* *growth* *factor* , Cyr61/Cef10, and neuroblastoma overexpressed gene) family, suppresses In vivo tumor growth and metastasis of K-1735 murine melanoma cells.
Hashimoto Y; Shindo-Okada N; Tani M; Nagamachi Y; Takeuchi K; Shiroishi T ; Toma H; Yokota J
Biology Division, National Cancer Center Research Institute, 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan.
Journal of experimental medicine (UNITED STATES) Feb 2 1998, 187 (3) p289-96, ISSN 0022-1007 Journal Code: I2V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We previously isolated a partial cDNA *fragment* of a novel gene, Elm1 (expressed in low-metastatic cells), that is expressed in low-metastatic but not in high-metastatic K-1735 mouse melanoma cells. Here we determined the full-length cDNA *structure* of Elm1 and investigated the effect of Elm1 expression on growth and metastatic potential of K-1735 cells. The Elm1 gene encodes a predicted protein of 367 amino acids showing approximately 40% amino acid identity with the CCN (connective tissue growth factor [CTGF], Cyr61/Cef10, neuroblastoma overexpressed gene [Nov]) family proteins, which consist of secreted cysteine-rich proteins with growth regulatory functions. Elm1 is also a cysteine-rich protein and contains a signal peptide and four domains conserved in the CCN family proteins. Elm1 was highly conserved, expressed ubiquitously in diverse organs, and mapped to mouse chromosome 15. High-metastatic K-1735 M-2 cells, which did not express Elm1, were transfected with an Elm1 expression vector, and several stable clones with Elm1 expression were established. The in vivo growth rates of cells expressing a high level of Elm1 were remarkably slower than those of cells expressing a low level of Elm1. Metastatic potential of transfectants was reduced in proportion to the level of Elm1 expression. Thus, Elm1 is a novel gene of CCN family that can suppress the in vivo growth and metastatic potential of K-1735 mouse melanoma cells.

4/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09336837 97312549 PMID: 9168990
Cloning of a mRNA preferentially expressed in chondrocytes by differential display-PCR from a human chondrocytic cell line that is identical with *connective* *tissue* *growth* *factor* (*CTGF*) mRNA.
Nakanishi T; Kimura Y; Tamura T; Ichikawa H; Yamaai Y; Sugimoto T; Takigawa M
Department of Biochemistry and Molecular Dentistry, Okayama University Dental School, Japan.
Biochemical and biophysical research communications (UNITED STATES) May 8 1997, 234 (1) p206-10, ISSN 0006-291X Journal Code: 9Y8 Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Chondrocyte- or chondrosarcoma cell line (HCS)-specific DNA *fragments* were obtained using differential display-PCR. Nucleotide sequences of 32 species derived from HCS cells were determined. One of the sequence

tags (tag no. 24) corresponded to the nucleotide sequence of connective tissue growth factor (CTGF). Northern blot analysis showed that CTGF was highly expressed in HCS cells and rabbit growth cartilage cells in culture but was not expressed in osteoblastic cells in culture. In situ hybridization revealed that CTGF was expressed only in the hypertrophic chondrocytes of costal cartilage and the vertebral column in embryonic mice. The expression of CTGF in HCS cells was up-regulated by the addition of TGF-beta or BMP-2. These findings suggest that CTGF participates in endochondral ossification.

4/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09142274 96265707 PMID: 9052988
A novel transforming growth factor beta response element controls the expression of the *connective* *tissue* *growth* *factor* gene.
Grotendorst GR; Okochi H; Hayashi N
Department of Cell Biology and Anatomy, University of Miami School of Medicine, FL 33136, USA.
Cell growth & differentiation (UNITED STATES) Apr 1996, 7 (4) p469-80, ISSN 1044-9523 Journal Code: AYH
Contract/Grant No.: GM37223, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We reported previously that transforming growth factor beta (TGF-beta) selectively induced high levels of connective tissue growth factor (CTGF) mRNA and protein in human skin fibroblasts. In this study, we investigated the molecular mechanism for TGF-beta regulation of CTGF gene expression. Northern blot and run-on transcription assays indicate that TGF-beta directly activates transcription of the CTGF gene. *Fragments* of the 5'flanking region of the human CTGF gene were linked to luciferase reporter constructs. TGF-beta induced a 25-30 fold increase in luciferase activity in NIH/3T3 fibroblasts that had been transfected with this construct compared with nontreated cells after 24 h incubation. Other growth factors, such as platelet derived growth factor or fibroblast growth factor, caused only a 2-3-fold induction. This response to TGF-beta occurred only in human skin fibroblasts, fetal bovine aortic smooth muscle cells, and NIH/3T3 fibroblasts but not in the epithelial cell lines tested. Analysis of deletion mutants indicated that an important TGF-beta regulatory element is located between positions -162 and -128 of the CTGF promoter sequence. A *fragment* of the promoter containing this region conferred TGF-beta induction to a SV40 enhanceriess promoter. Methylation interference and competition gel shift assays mapped a unique 13-nucleotide sequence delineating a novel TGF-beta cis-regulatory element. Point mutations in this region result in a complete loss of the TGF-beta induction, identifying this sequence as a new TGF-beta response element.

4/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08075927 93327926 PMID: 7687569
The modular architecture of a new family of growth regulators related to *connective* *tissue* *growth* *factor*.
Bork P
Max-Delbruck-Centre for Molecular Medicine, Berlin-Buch, Germany.
FEBS letters (NETHERLANDS) Jul 26 1993, 327 (2) p125-30, ISSN 0014-5793 Journal Code: EUH
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Recently, several groups have characterized and sequenced members of a new family of growth regulators (originally called cef10, connective tissue growth factor, fisp-12, cyr61, or, alternatively, beta IG-M1 and beta IG-M2), all of which belong to immediate-early genes expressed after induction by growth factors or certain oncogenes. Sequence analysis of this family revealed the presence of four distinct modules. Each module has homologues in other extracellular mosaic proteins such as Von Willebrand factor, slit, thrombospondins, fibrillar collagens, IGF-binding proteins and mucins. Classification and analysis of these modules suggests the location of binding regions and, by analogy to better characterized modules in other proteins, sheds some light onto the *structure* of this new family.

4/3,AB/18 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13198484 BIOSIS NO.: 200100405633
Type II alveolar epithelial cells and interstitial fibroblasts express *connective* *tissue* *growth* *factor* in IPF.
AUTHOR: Pan L-H; Yamauchi K; Uzuki M; Nakanishi T; Takigawa M; Inoue H; Sawai T(a)
AUTHOR ADDRESS: (a)First Dept of Pathology, Iwate Medical University School of Medicine, Uchimaru 19-1, Morioka, 020-8505**Japan
JOURNAL: European Respiratory Journal 17 (6):p1220-1227 June, 2001 MEDIUM: print
ISSN: 0903-1936
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Connective tissue growth factor (CTGF) is a growth and chemotactic factor for fibroblasts encoded by an immediate early gene that is transcriptionally activated by transforming growth factor-beta. Previous studies have shown that both CTGF messenger ribonuclear acid (mRNA) and protein are expressed in renal fibrosis and bleomycin-induced pulmonary fibrosis in mice. The aim of the present study was to investigate the localization of CTGF protein and its mRNA expression in the fibrotic lung tissue of patients with idiopathic pulmonary fibrosis (IPF). Using human fibrotic lung tissue obtained from eight autopsy cases and four biopsy cases with IPF, immunohistochemical staining, in situ hybridization, and reverse transcription-polymerase chain reaction (RT-PCR) were performed. The cellular immunoreactivity for CTGF was markedly increased in the lung tissue of patients with IPF, compared to normal lungs. The immunolocalization of CTGF was confined predominantly to proliferating type II alveolar epithelial cells and activated fibroblasts. In the normal lung, type II alveolar epithelial cells stained for CTGF were sparsely distributed. CTGF mRNA was localized in proliferating type II alveolar epithelial cells and activated fibroblasts in the interstitium of fibrotic lung tissues. RT-PCR analysis showed that CTGF mRNA was expressed at a higher level in fibrotic lungs than in normal lungs. In both an autocrine and a paracrine manner, type II alveolar epithelial cells and activated

fibroblasts may play a critical role in pulmonary fibrosis by producing connective tissue growth factor which modulates fibroblast proliferation and extracellular matrix production.

2001

4/3,AB/19 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13146940 BIOSIS NO.: 200100354089
Connective *tissue* *growth* *factor*.
AUTHOR: Grotendorst Gary R; Bradham Douglas M(a)
AUTHOR ADDRESS: (a)Baltimore, MD**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1243 (3):pNo Pagination Feb. 20, 2001
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The invention relates to a method of producing connective tissue growth factor (CTGF). A method of the invention can be performed, for example, by transforming a host cell with a polynucleotide encoding a CTGF polypeptide having an amino acid sequence of SEQ ID NO: 2 or an active *fragment* thereof; and growing the host cells under conditions suitable for expressing the polynucleotide in the host cell. In an embodiment, the method further involves isolating the CTGF polypeptide or the active *fragment*. The invention also relates to a method for producing a vector containing a polynucleotide encoding a CTGF polypeptide or an active *fragment* thereof by inserting a polynucleotide encoding a CTGF polypeptide having an amino acid sequence of SEQ ID NO: 2 or a variant thereof into the vector. The vector can be an expression vector, for example, a plasmid expression vector or a viral expression vector. In an embodiment, the polynucleotide has a nucleotide sequence of SEQ ID NO: 1 or a variant thereof.

2001

4/3,AB/20 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13082170 BIOSIS NO.: 200100289319
Rho-dependent inhibition of the induction of *connective* *tissue* *growth* *factor* (*CTGF*) by inhibitors of HMG CoA reductase (statins).
AUTHOR: Eberlein M(a); Heusinger-Ribeiro J(a); Goppelt-Struebe M(a) AUTHOR ADDRESS: (a)Medizinische Klinik IV, Universitaet Erlangen-Nuernberg, Loschgestrasse 8, D-91054, Erlangen**Germany
JOURNAL: Naunyn-Schmiedeberg's Archives of Pharmacology 363 (4 Supplement):pR64 2001
MEDIUM: print
CONFERENCE/MEETING: 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology Mainz, Germany March 13-15, 2001
SPONSOR: German Society for Experimental and Clinical Pharmacology and Toxicology
ISSN: 0028-1298
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English
2001

4/3,AB/21 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13036738 BIOSIS NO.: 200100243887
CTGF and SMADs, maintenance of scleroderma phenotype is independent of SMAD signaling.
AUTHOR: Holmes Alan; Abraham David J; Sa Susan; Shiwen Xu; Black Carol M; Leask Andrew(a)
AUTHOR ADDRESS: (a)FibroGen, Inc., 225 Gateway Blvd., South San Francisco, CA, 94080: aleask@fibrogen.com**USA
JOURNAL: Journal of Biological Chemistry 276 (14):p10594-10601 April 6, 2001
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: In normal adult fibroblasts, transforming growth factor-beta (TGFbeta) induces the expression of connective tissue growth factor (CTGF). CTGF independently promotes fibroblast proliferation and matrix deposition, and in acute models of fibrosis promotes cell proliferation and collagen deposition acting synergistically with TGFbeta. In contrast to normal fibroblasts, fibroblasts cultured from fibrotic tissues express high basal levels of CTGF, even in the absence of added TGFbeta. Induction of transcription by TGFbeta requires the action of SMAD proteins. In this report we have investigated the role of SMADs in the TGFbeta-induction of CTGF in normal fibroblasts and in the elevated levels of CTGF expression found in dermal fibroblasts cultured from lesional areas of patients with scleroderma, a progressive fibrotic disorder that can affect all organs of the body. We have identified a functional SMAD binding site in the CTGF promoter. TGFbeta-induction of CTGF is dependent on SMAD3 and SMAD4 but not SMAD2 and is p300-independent. However, mutation of the SMAD binding site does not reduce the high level of CTGF promoter activity observed in dermal fibroblasts cultured from lesional areas of scleroderma patients. Conversely, the previously termed TGFbetaRE in the CTGF promoter is required for basal CTGF promoter activity in normal fibroblasts and for the elevated level of CTGF promoter activity in scleroderma fibroblasts. Thus, the maintenance of the fibrotic phenotype in scleroderma fibroblasts, as visualized by excess CTGF expression, appears to be independent of SMAD-dependent TGFbeta signaling. Furthermore, given CTGF's activities, the high level of CTGF expression observed in scleroderma lesions may contribute to the excessive scarring observed in this disorder.

2001

4/3,AB/22 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

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12679471 BIOSIS NO.: 200000432973
CTGF (IGFBP-rP2) is specifically expressed in malignant lymphoblasts of patients with acute lymphoblastic leukaemia (ALL).
AUTHOR: Vorwerk P(a); Wex H; Hohmann B; Oh Y; Rosenfeld R G; Mittler U AUTHOR ADDRESS: (a)Department of Pediatric Hematology and Oncology, Otto von Guericke University Magdeburg, E.-Larisch-Weg 17-19, D-39112, Magdeburg**Germany
JOURNAL: British Journal of Cancer 83 (6):p756-760 September, 2000 MEDIUM: print
ISSN: 0007-0920
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Connective tissue growth factor (CTGF) is a major chemotactic and mitogenic factor for connective tissue cells. The amino acid sequence shares an overall 28-38% identity to IGFBPs and contains critical conserved sequences in the amino terminus. It has been demonstrated that human CTGF specifically binds IGFs with low affinity and is considered to be a member of the IGFBP superfamily (IGFBP-rP2). In the present study, the expression of CTGF (IGFBP-rP2) in human leukaemic lymphoblasts from children with acute lymphoblastic leukaemia (ALL) was investigated. RNA samples from tumour clones enriched by ficoll separation of bone marrow or peripheral blood mononuclear cells (MNC) from 107 patients with childhood ALL at diagnosis and 57 adult patients with chronic myeloid leukaemia (CML) were studied by RT-PCR. In addition MNC samples from children with IDDM and cord blood samples from healthy newborns were investigated as control groups. Sixty-one percent of the patients with ALL (65 of 107) were positive for CTGF (IGFBP-rP2) expression. In the control groups, no expression of CTGF (IGFBP-rP2) in peripheral MNC was detected, and in the group of adult CML patients only 3.5% (2 of 57) were positive for this gene. The role of CTGF (IGFBP-rP2) in lymphoblastic leukaemogenesis requires further evaluation, as does its potential utility as a tumour marker.

2000

4/3,AB/23 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12659652 BIOSIS NO.: 200000413154
A novel RNA element that confers post-transcriptional repression of human *connective* *tissue* *growth* *factor*/hypertrophic chondrocyte specific 24 (*ctgf*/hcs24) gene.
AUTHOR: Kubota S(a); Kondo S(a); Eguchi T(a); Hattori T(a); Nakanishi T(a); Pomerantz R J; Takigawa M(a)
AUTHOR ADDRESS: (a)Biochemistry, Okayama University Dental School, Okayama **Japan
JOURNAL: Journal of Bone and Mineral Research 15 (Suppl. 1):pS340 September, 2000
MEDIUM: print
CONFERENCE/MEETING: Twenty-Second Annual Meeting of the American Society for Bone and Mineral Research Toronto, Ontario, Canada September 22-26, 2000
SPONSOR: American Society for Bone and Mineral Research
ISSN: 0884-0431
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English
2000

4/3,AB/24 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

12017647 BIOSIS NO.: 199900298166
The *connective* *tissue* *growth* *factor*/cysteine-rich 61/nephroblastoma overexpressed (CCN) family.
AUTHOR: Brigstock David R(a)
AUTHOR ADDRESS: (a)Wexner Institute for Pediatric Research, Children's Hospital, 700 Children's Drive, Columbus, OH**USA
JOURNAL: Endocrine Reviews 20 (2):p189-206 April, 1999
ISSN: 0163-769X
DOCUMENT TYPE: Literature Review
RECORD TYPE: Citation
LANGUAGE: English
1999

4/3,AB/25 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

11738161 BIOSIS NO.: 199800379987
Immunohistochemical localization of *connective* *tissue* *growth* *factor* in human endometrium and decidua.
AUTHOR: Uzumcu M(a); Al-Homsi M F; Brigstock D R; Ayberk H; Coskun S; Jaroudi K; Hollanders J M G
AUTHOR ADDRESS: (a)Dep. Biol. Med. Res., King Faisal Specalist Hosp. Res. Cent., Riyadh**Saudi Arabia
JOURNAL: Biology of Reproduction 58 (SUPPL. 1):p197 1998
CONFERENCE/MEETING: Thirty-first Annual Meeting of the Society for the Study of Reproduction College Station, Texas, USA August 8-11, 1998 SPONSOR: Society for the Study of Reproduction
ISSN: 0006-3363
RECORD TYPE: Citation
LANGUAGE: English
1998
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Set Items Description
S1 488 (CONNECTIVE()TISSUE()GROWTH()FACTOR OR CTGF) S2 340 (CONNECTIVE()TISSUE()GROWTH()FACTOR OR CTGF)/TI S3 37 S2 AND (STRUCTURE OR FRAGMENT?)
S4 25 RD (unique items)
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340 S2
248575 STRUCTURE/TI
53323 FRAGMENT?/TI
S5 2 S2 AND (STRUCTURE OR FRAGMENT?)/TI
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5/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09802884 98326297 PMID: 9661651
Identification of glycosylated 38-kDa *connective* *tissue* *growth* *factor* (IGFBP-related protein 2) and proteolytic *fragments* in human biological fluids, and up-regulation of IGFBP-rP2 expression by TGF-beta in Hs578T human breast cancer cells. Yang DH; Kim HS; Wilson EM; Rosenfeld RG; Oh Y
Dept. of Pediatrics NRC5, Oregon Health Sciences University, Portland 97201, USA.
Journal of clinical endocrinology and metabolism (UNITED STATES) Jul 1998, 83 (7) p2593-6, ISSN 0021-972X Journal Code: HRB Contract/Grant No.: CA 58110, CA, NCI; DK51513, DK, NIDDK Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Connective Tissue Growth Factor (CTGF) is a cysteine-rich peptide involved in human atherosclerosis and fibrotic disorders such as scleroderma. CTGF has considerable N-terminal sequence similarity with the insulin-like growth factor binding proteins (IGFBPs), including preservation of cysteines, and has been postulated to be a member of the IGFBP superfamily. Indeed, recent studies have shown that baculovirus generated CTGF, a secreted 38-kDa protein, binds IGFs in a specific manner, leading to the provisional renaming of CTGF as IGFBP-8 (or IGFBP-rP2). With immunoprecipitation and immunoblotting, using polyclonal anti-IGFBP-rP2 antibody generated against recombinant human IGFBP-rP2bac, IGFBP-rP2 can be identified in the serum-free conditioned media of Hs578T human breast cancer cells, as well as in various human biological fluids, such as normal sera, pregnancy sera, and cerebrospinal, amniotic, follicular and peritoneal fluids. Glycosylation studies with endoglycosidase F reveal that endogenous human IGFBP-rP2 is a secreted, glycosylated, approximately 32-38-kDa protein with 2-8-kDa of N-linked sugars and a 30-kDa core. There are 18- and 24-kDa proteins that appear to be IGFBP-rP2 degradation products. In Hs578T human breast cancer cells, transforming growth factor (TGF)-beta 2, a potent growth inhibitor for these cells, upregulates IGFBP-rP2 mRNA and protein levels. Expression of Hs578T IGFBP-rP2 is significantly increased by TGF-beta 2 treatment in a dose-dependent manner, with 2.5- and 6-fold increases in mRNA and protein levels, respectively, at a TGF-beta 2 concentration of 10 ng/ml. Our studies indicate that IGFBP-rP2 appears to be an important endocrine factor, and one of the critical downstream effectors of the critical downstream effectors of TGF-beta, similar to the role of IGFBP-3 in TGF-beta-induced growth inhibition in human breast cancer cells.
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5/3,AB/2 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

11579592 BIOSIS NO.: 199800360288
Identification of glycosylated 38-kDa *connective* *tissue* *growth* *factor* (IGFBP-related protein 2) and proteolytic *fragments* in human biological fluids, and up-regulation of IGFBP-rP2 expression by TGF-beta in Hs578T human breast cancer cells. AUTHOR: Yang Doo-Hyun; Kim Ho-Seong; Wilson Elizabeth M; Rosenfeld Ron G; Oh Youngman
AUTHOR ADDRESS: Dep. Pediatr. NRC5, Oreg. Health Sci. Univ., 3181 SW Sam Jackson Park Rd., Portland, OR 97201**USA
JOURNAL: Journal of Clinical Endocrinology & Metabolism 83 (7):p2593-2596 July, 1998
ISSN: 0021-972X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Connective Tissue Growth Factor (CTGF) is a cysteine-rich peptide involved in human atherosclerosis and fibrotic disorders such as scleroderma. CTGF has considerable N-terminal sequence similarity with the insulin-like growth factor binding proteins (IGFBPs), including preservation of cysteines, and has been postulated to be a member of the IGFBP superfamily. Indeed, recent studies have shown that baculovirus generated CTGF, a secreted 38-kDa protein, binds IGFs in a specific manner, leading to the provisional renaming of CTGF as IGFBP-8 (or IGFBP-rP2). With immunoprecipitation and immunoblotting, using polyclonal anti-IGFBP-rP2 antibody generated against recombinant human IGFBP-rP2bac, IGFBP-rP2 can be identified in the serum-free conditioned media of Hs578T human breast cancer cells, as well as in various human biological fluids, such as normal sera, pregnancy sera, and cerebrospinal, amniotic, follicular and peritoneal fluids. Glycosylation studies with endoglycosidase F reveal that endogenous human IGFBP-rP2 is a secreted, glycosylated, approximately 32-38kDa protein with 2-8-kDa of N-linked sugars and a 30-kDa core. There are 18- and 24-kDa proteins that appear to be IGFBP-rP2 degradation products. In Hs578T human breast cancer cells, transforming growth factor (TGF)-beta2, a potent growth inhibitor for these cells, upregulates IGFBP-rP2 mRNA and protein levels. Expression of Hs578T IGFBP-rP2 is significantly increased by TGF-beta2 treatment in a dose-dependent manner, with 2.5- and 6-fold increases in mRNA and protein levels, respectively, at a TGF-beta2 concentration of 10 ng/ml. Our studies indicate that IGFBP-rP2 appears to be an important endocrine factor, and one of the critical downstream effectors of TGF-beta, similar to the role of IGFBP-3 in TGF-beta-induced growth inhibition in human breast cancer cells.

1998
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Set Items Description
S1 488 (CONNECTIVE()TISSUE()GROWTH()FACTOR OR CTGF) S2 340 (CONNECTIVE()TISSUE()GROWTH()FACTOR OR CTGF)/TI S3 37 S2 AND (STRUCTURE OR FRAGMENT?)
S4 25 RD (unique items)
S5 2 S2 AND (STRUCTURE OR FRAGMENT?)/TI
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12sep01 16:53:13 User217743 Session D535.4
$1.69 0.529 DialUnits File155
$3.60 18 Type(s) in Format 4 (UDF)
$3.60 18 Types
$5.29 Estimated cost File155

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$6.60 4 Type(s) in Format 3 (UDF)
$8.25 5 Type(s) in Format 4 (UDF)
$14.85 9 Types
$24.00 Estimated cost File5
OneSearch, 2 files, 2.163 DialUnits FileOS
$0.20 TYMNET
$29.49 Estimated cost this search
$31.67 Estimated total session cost 4.063 DialUnits
Logoff: level 01.08.22 D 16:53:13